éggagagec ceggagtgag eggagtageg agteggeaae eeggaggggt agaaatattt 60 ctate ata get cat tea and act agg ace ant got gga and att aca tot 110 Met Ala His Ser Lys Thr Arg Thr Asn Asp Gly Lys Ile Thr Tyr ccg cct ggg gtc aag gaa ata tca gat aaa ata tct aaa gag gag atg 158 Pro Pro Gly Val Lys Glu Ile Ser Asp Lys Ile Ser Lys Glu Glu Met 20 25 30 206 gtg aga cga tta aag atg gtt gtg aaa act ttt atg gat atg gac cag Val Arg Arg Leu Lys Met Val Val Lys Thr Phe Met Asp Met Asp Gln 35 40 gac tot gaa gaa gaa aag gag ott tat tta aac ota got tta cat ott 254 Asp Ser Glu Glu Glu Lys Glu Leu Tyr Leu Asn Leu Ala Leu His Leu 50 55 gct tca gat ttt ttt ctc aag cat cct ggt aaa gat gtt cgc tta ctg 302 Ala Ser Asp Phe Phe Leu Lys His Pro Gly Lys Asp Val Arg Leu Leu 65 70 gta gcc tgc tgc ctt gct gat att ttc agg att tat gct cct gaa gct 350 Val Ala Cys Cys Leu Ala Asp Ile Phe Arg Ile Tyr Ala Pro Glu Ala 80 85 cct tac aca tcc cct gat aaa cta aag gat ata ttt atg ttt ata aca 398 Pro Tyr Thr Ser Pro Asp Lys Leu Lys Asp Ile Phe Met Phe Ile Thr 100 105 110 446 aga cag ttg aag ggg cta gag gat aca aag agc cca caa ttc aat agg Arg Gln Leu Lys Gly Leu Glu Asp Thr Lys Ser Pro Gln Phe Asn Arg 115 120 125 tat ttt tat tta ctt gag aac att gct tgg gtc aag tca tat aac ata 494 Tyr Phe Tyr Leu Leu Glu Asn Ile Ala Trp Val Lys Ser Tyr Asn Ile 130 135 140 542 tgc ttt gag tta gaa gat agc aat gaa att ttc acc cag cta tac aga Cys Phe Glu Leu Glu Asp Ser Asn Glu Ile Phe Thr Gln Leu Tyr Arg 150 155 145

DEC 0 1. 2005

acc Thr 160	tta Leu	ttt Phe	tca Ser	gtt Val	ata Ile 165	aac Asn	aat Asn	ggc Gly	cac His	aat Asn 170	cag Gln	aạa Lys	gtc Val	cat His	atg Met 175	590
cac His	atg Met	gta Val	gac Asp	ctt Leu 180	atg Met	agc Ser	tct Ser	att Ile	att Ile 185	tgt Cys	gaa Glu	ggt Gly	gat Asp	aca Thr 190	gtg Val	638
tct Ser	cag Gln	gag Glu	ctt Leu 195	ttg Leu	gat Asp	acg Thr	gtt Val	tta Leu 200	gta Val	aat Asn	ctg Leu	gta Val	cct Pro 205	Ala	cat His	686
aag Lys	aat Asn	tta Leu 210	aac Asn	aag Lys	caa Gln	gca Ala	tat Tyr 215	gat Asp	ttg Leu	gca Ala	aag Lys	gct Ala 220	tta Leu	ctg Leu	aag Lys	734
agg Arg	aca Thr 225	gct Ala	caa Gln	gct Ala	att Ile	gag Glu 230	cca Pro	tat Tyr	att Ile	acc Thr	act Thr 235	ttt Phe	ttt Phe	aat Asn	cag G1n	782
gtt Val 240	ctg Leu	atg Met	ctt Leu	ggg Gly	aaa Lys 245	aca Thr	tct Ser	atc Ile	agc Ser	gat Asp 250	ttg Leu	tca Ser	gag Glu	cat His	gtc Val 255	830
ttt Phe	gac Asp	tta Leu	att Ile	ttg Leu 260	gag Glu	ctc Leu	tac Tyr	aat Asn	att Ile 265	gat Asp	agt Ser	cat His	ttg Leu	ctg Leu 270	ctc Leu	878
tct Ser	gtt Val	tta Leu	ccc Pro 275	cag Gln	ctt Leu	gaa Glu	ttt Phe	aaa Lys 280	tta Leu	aag Lys	agc Ser	aat Asn	gat Asp 285	Asn	gag Glu	926
gag Glu	cgc Arg	cta Leu 290	Gln	gtt Val	gtt Val	aaa Lys	cta Leu 295	Leu	gca Ala	aaa Lys	atg Met	ttt Phe 300	Gly	gca Ala	aag Lys	974
gat Asp	tca Ser 305	Glu	ttg Leu	gct	tct Ser	caa Gln 310	Asn	aag Lys	cca Pro	ctt Leu	tgg Trp 315	Gln	tgc Cys	tac Tyr	ttg Leu	1022
ggc Gly 320	/ Arc	ttt Phe	aat Asr	gat Asp	ato Ile 325	His	gta Val	cca Pro	ato Ile	cgc Arg 330	, Leu	gaa Glu	tgt Cys	gtg Val	aaa Lys 335	1070

	-	_		_		atg Met		His		_		_		_	Leu	1118
						agg Arg			_			_	-		-	1166
	_	_		_		ata Ile	-		-	-		_	_			1214
Leu			-			ctt Leu 390				-		-			-	1262
						aaa Lys										1310
	_			_		cag G1n		-	-			_	_			1358
						gac Asp										1406
-		_		_		ctt Leu	-	_				_			_	1454
						act Thr 470										1502
-				-	-	tta Leu					-	-		-		1550
						ctc Leu										1598

		aag Lys														1646
		atg Met 530						Leu								1694
gat Asp	ttc Phe 545	atg Met	aag Lys	aaa Lys	ttc Phe	aca Thr 550	cag Gln	gtg Val	tta Leu	gaa Glu	gat Asp 555	gat Asp	gag Glu	aaa Lys	ata Ile	1742
		cag Gln														1790
		ggt Gly														1838
		aca Thr														1886
	Ala	cct Pro 610														1934
		aac Asn														1982
_		act Thr	-		_	Пe	_				_	•		_	gta Val 655	2030
		ttt Phe														2078
		ctg Leu								_		_	_	_	-	2126

gca c Ala L	₋eu (2174
cca c Pro H 7			_		-	_			-						2222
aaa g Lys G 720						-			_						2270
ata t Ile P			Ser					Phe					Glu		2318
cat a His L	-	Ser		_		_		_	-					_	2366
gtt a Val T	[hr]					_			-		_			 -	2414
cct t Pro T 7															2462
aat g Asn A 800							-						-	-	2510
gaa g Glu G					-		_	_		Пe	_	_			2558
atg g Met V		Arg													2606
act t Thr S	Ser T									_					2654

_		_	_				_	aaa Lys		-	_		-	-	·	2702
	-	•		_	-			aag Lys	_	_	Gln	-		_		2750
	-					_		tat Tyr	_		•	•		_	Ile	2798
	_	-	-			_	_	caa Gln 920			_	_			cac His	2846
•				_				cca Pro		_		_			-	2894
_		_	-	-	_		_	aag Lys			_			_		2942
	-	_	-					gta Val			Glu		-	_	cag Gln 975	2990
	-	-	_		_			ttg Leu							_	3038
							Leu	gca Ala 1000				Asp			aaa Lys	3086
_	Gln	•		_		Leu		gat Asp	_		Ğlu	_				3134
Val	_	_			Met	_		aat Asn	_	Asn		_		_		3182

	Arg			Val										Gln		3230
cca Pro	_	_	Āla		_		-	Lys	-				Cys	_		3278
gcc Ala	_	Asn			-		Lys	-				Ser				3326
cct Pro	Lys					Pro					Thr					3374
aat Asn 1		-			Lys		Tyr	_		Pro	-					3422
ttc Phe 1120	Thr			Lys					Asn	-				Val		3470
	cca Pro		Ser		Ala			Gln					Ser			3518
_	gaa Glu	Thr	-				Ser					Pro				3566
	Arg					Leu					Met				gaa Glu	3614
Asn	gaa Glu 1185				Met					Pro						3662
	aga Arg O			Ser					Ser		Leu			Pro		3710

FIG. I-7

ggc Gly	agg Arg	aaa Lys	Lys	acg Thr 1220	Pro	gtc Val	aca Thr	Glu	cag Gln 1225	gag Glu	gag Glu	aaa Lys	Leu	ggt Gly 1230	atg Met	3758
gat Asp	gac Asp	Leu	act Thr 1235	aag Lys	ttg Leu	gta Val	Gln	gaa Glu 1240	cag Gln	aaa Lys	cct Pro	Lys	ggc Gly 1245	agt Ser	cag Gln	3806
cga Arg	Ser	cgg Arg L250	aaa Lys	aga Arg	ggc Gly	His	acg Thr 1255	gct Ala	tca Ser	gaa Glu	tct Ser	gat Asp 1260	gaa Glu	cag Gln	cag Gln	3854
Trp					Arg					Ile	tta Leu L275					3902
	Gln			Pro					Lys		ggc			Pro		3950
cct Pro	ctt Leu	ggt Gly	Gly	ggt Gly 1300	aca Thr	cca Pro	aaa Lys	Glu	gag G1u 1305	cca Pro	aca Thr	atg Met	Lys	act Thr 1310	tct Ser	3998
aaa Lys	aaa Lys	Gly	agc Ser 1315	Lys	aaa Lys	aaa Lys	Ser	gga Gly 1320	cct Pro	cca Pro	gca Ala	Pro	gag Glu 1325	Glu	gag Glu	4046
gaa Glu	Glu	gaa Glu 1330	gaa Glu	aga Arg	caa Gln	Ser	gga Gly 1335	aat Asn	acg Thr	gaa Glu	cag Gln	aag Lys 1340	tcc Ser	aaa Lys	agc Ser	4094
Lys					Ser					Gln	aga Arg 1355				cct. Pro	4142
gaa Glu 136	Ser	agt Ser	gca Ala	Ile	gaa Glu 1365	tcc Ser	aca Thr	cag Gln	Sen	aca Thr 1370	cca Pro	cag Gln	aaa Lys	Gly	cga Arg 1375	4190
gga Gly	aga Arg	cca Pro	Ser	aaa Lys 1380	Thr	cca Pro	tca Ser	Pro	tca Ser 1385	caa Gln	cca Pro	aaa Lys	Lys	aat Asn 1390	gtg Val	4238

taagttgtaa atattacatt tcaaaccaat ttcaaattat tttgcaaaag ttcctaaatt 4298 End

tgtaaacata catattgctg tatttaaatt ccatatattt agccccatta cactaggtac 4358 ggcggcgaag tgctaaaagg gaacggcgat gaacaaatgt aattaataac tttctctgtg 4418 aaagctttgg aaaaatcttt ttttttttt ttttttttg gtcaagcttg aggctgaata 4478 aagcctttga tgcacaaaat gggactgctg aagagtggac agttggacct tactttggtg 4538 accccataca tttgtggtca catgctttag ccatacacat ggtaacattg actatggagt 4598 cttgtgaaag tgtaatgtgc gatggctatg tagacataaa gaagaaactt gtaaatatct 4658 tttttctttt ttttaatgtt tctgatttct gaagtgcttg tatagctttt atctgcggct 4718 ttaaactgac agtacccgac tgtttattgg atctattgat ttgaaaagaa tttgttagga 4778 tagatettaa geagtaatet geeagtgett geattegeat ettetgeaat etteategea 4838 aaaaaaattt gttttcaaca attggtgtca ttttcttgat gtcactattt gttggagagt 4898 taaatggtct cttccctttg tgtatcttac ctagtgttta ctcctgggca cccttaatct 4958 tcagaggtgc taaattgtct gccattacac cagaaggatg cctctgatag gaggacaacc 5018 atgcaaattg tgaaatagtc ctgaagttct tggattactt tacacctcag tattgatttg 5078 tcccagaatt ttctggcctt tcatggcaat gaaaatttta agaagaaaga tttaaagtat 5138 tttaatttta aagagtgtgt tataaaaataa tgtactgaat tetttateee attttateat 5198 cctttcagtt tttattaatc tactgtatca ataaaattct gtaatttgaa tgagtaaaaa 5258 5271 ааааааааа ааа



LYLNLALHLASDFFLKHPGKD**V**RLLV 196 217 LDTVLVNLVPAHKNLNKQAYDL

LYLNLALHLASDFFLKHPGKDVRLLVACCLADIFRTYAPEAPYTSPDKLKDIFMFTTRQLKGL

LMLGKTSISDLSEHVFDLILELYNIDSHLLLSVLPQL

LGRFNDIHVPIRLECVKFASHCLMNHPDLAKDLTEYL 355 VTAAKKDILLVNDHLLNFVRERTLDKRWRV 404

FIG. 2

β–strand	M_{g} -ATP binding loop $(G \times G \times G \times V)$	β-strand 2	β -strand 3 (x x x K x x x)	α -helix C $(x \times x \times E \times x \times)$
	426	453	472	489
YALQ.SA	GKDAAKQI	LLVERIF	ERM K CLYYLYA	VKALN E MWKC
YTLGVSA (Elm 1)	GeDrfGkV (Ror2)	LLYELMD (Yk1516)		QAFKN K MQVL (Araf)
YALLNLL (Tsl)	GsGsfGdI (CKla)	YLGEQVS (PKN2)	YAM K CLDKKRI (bARKI)	TLALN E RIML (bARKI)
YHIKQNI (Cdc15)	AeGesHiS (Ypka)	YLCLCLN (BCK1)	YAM K CLDKKRI (DmGPRKI)	TTRVR E IKFI (SMEI)
YKLVRKI (CKla	HeSdfSeV (Mik1)		VAI K CIAKKAL (CamK1)	
IVLQESI (Alk5)				
	Consensus: β-strand AS3 position: 419 AS3 sequence: YALQ.SA Similar YTLGVSA (Elm 1) protein YALLNLL (Tsl) kinase YKLVRKI (CK1s) sequences: YKLVRKI (CK1a IVLQESI (Alk5)	trand Q.SA .GVSA (Elm 1) .LNLL (Tsl) .KQNI (Cdc15) .VRKI (CK1a .QESI (Alk5)	trand Mg-ATP binding loop (G x G x x G x V) 426 Q.SA GKDAAKQI GKDAAKQI GVSA (Elm 1) GeDrfGkV (Ror2) LINLL (Tsl) GsGsfGdI (CK1a) LVRKI (CK1a HeSdfSeV (Mik1) QESI (Alk5)	trand Mg-ATP binding loop (G x G x x G x V) β-strand 2 β-strand 3 (x x x K x x x) Q.SA GKDAAKQI LLVERIF 472 GVSA (Elm 1) GeDrfGkV (Ror2) LLYELMD (Yk1516) YAM K CLKKDVI (CeTPA1) LKQNI (Cdc15) GeGsfGdI (CK1a) YLGEQVS (PKN2) YAM K CLKKDVI (CeTPA1) VRKI (CK1a) HeSdfSeV (Mik1) YLCLCLN (BCK1) YAM K CLKKRI (DmGPRK1) QESI (Alk5) VAI K CLAKKAL (CamK1)

regions:

Subdomain

Subdomain II

Subdomain III

conserved

Hank's

Hank's

conserved

regions:

AS3 sequence: AS3 position:

sequences: protein kinase

Consensus: 509 β-strand 4

LLDWFERP (Pim1) LLDIVKDP (TPCKII)

525

Similar

Subdomain IV

LLDIVKDP

LVKLIGYC (APK1) LLGLCREA (Klg)

Subdomain V

IFSK.VMV β-strand 5 α-helix D 540

GKAQDEMKK

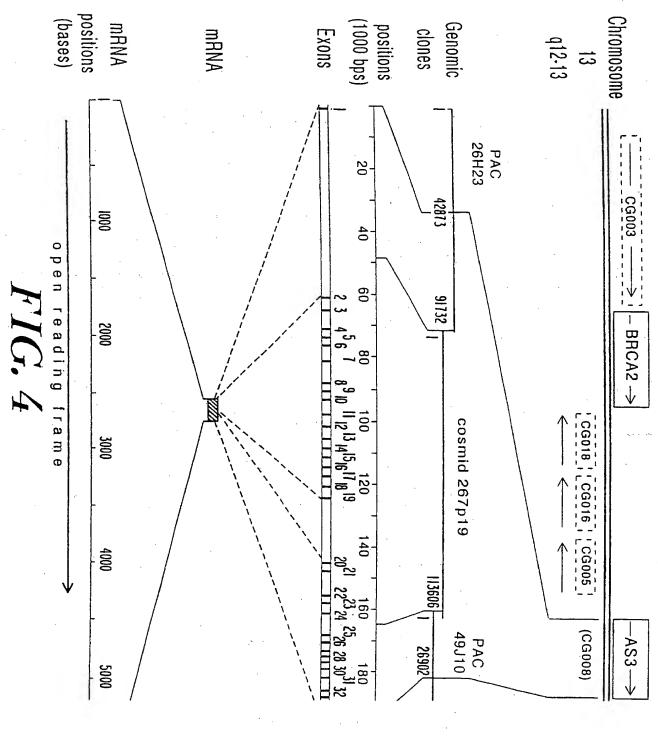
IFSCLVME (PvpK1) KFSCLVME (G11a)

KFSCLVME (ZmPPK) GNLQEYLTR (TGFbRII) GNLQNFLKL (Let23)
GSLQNFLRE (TORSO)

Subdomain VIa

EDDEKIRKQ.LEVI 554 α-helix E

ECDANIMKQILSG (PICPK) ADQLNIAKQISAG (TORRTK) ERDADAVKQILEA (CaMKIV) ESVIMYTKQLLL (NPK1)



{42873}	1 CCGGAGAG	Exon 1ACCCGG	46 {42919} AG * gtaggaa
(13347) ttttcttgtttcag *			73 (13475) AG * gtgagta
(16397) ttttatttttgtatag *			77 (16602) AG * gcaagta
(22832) tcttttttttatttaag *	378 GATATATT		54 (22920) AG * gtaagca
(23028) ccttatttttag *	465 AACATTGC	56 Exon 5GTTATA	52 (23125) WA * gtaagtt
(23747) ttttgaattgcag *		Exon 6CTCATA	39 (23873) AG * gtgagta
(32357) tttatgtttttcag *	690 AATTTAAA	Exon 7TTACCAC	54 (32439) CT * gtaagtc
(37809) ctttctcctcaaaag *			11 (37951) AG * gtaactt
(40437)ttttattttag *	912 AGCAATGA		
(43428) tttatattttatcag *			22 (43524) AG * gtactat
(48471)tgttatctttcag *			58 (48617) GA * gtaagta
(51727) ttttttgtttttaag *			20 (51880) CG * gtaagtt
(53049) tctgcttttttgtag *			34 (53164) WA * gtatgtt

FIG. 5-1

(58816) tttgtgtttttcag *	1535 AGCATTGA	Exor	14AAC	1616 CCAAA	(58898) * gtaagta
(61447) ttgtgtgatttacag *	1617 ACAGATGC	Exor	ı 15TAT	1665 TACAA	(61497) * gtaagtt
(64323) tttattttaag *	1666 GAAATTTA	Exon	16GTT	1805 GTGTG	(64464) * gtaagga
(65916) taatctgtattacag *	1806 CGTGAAAT	Exon	17TCT	1921 ATCAG	(66033) * gtatttg
(71527) ttggtcatattttag *		Exon	18TGC	2027 TTAAG	(71633) * gtaagta
(74539) tgattcattttatag *	2028 GTACTCTC	Exon	19ATC	2188 AGATC	(74700) * gtgagtt
(96694) tttttttttaatag *		Exon	20TAT	2312 TTGAG	(96818) * gtaatga
(99765) tcccctcattttcag *	2313 CCTCTGCA	Exon	21ATG/	2471 ATCGG	(99925) * gtaattt
(105674) ctcgtttatttttag *	2472 CTTCCAGG	Exon	22TGG	2540 ГСААА	(105744) * gtgagta
(107185) ttgtctcttaaatag *				2677 ATTAG ?	(107322) * gtatgca
(110571) ctactcatttttcag *	2678 TAAACCAG	Exon	24CTA	2801 CCAAC ³	(110696) * gtaagga
[4319] ttgtgtctttacag *	2802 GATGAATG	Exon	25TGT	3006 FAGTG	[4524] * gtaagca

FIG. 5-2

[6829] * ttttctttttcag.	3007 AAAAATTA	Exon	3121 26GTTAAAGA	[6945] * gtaagac
[9074] ttttttttttttag *	3122 ATGTCTTT	Exon	3254 27TGAATGAA	[9208] * gtatgta
[9522] tatactattgcag *	3255 AAACTGTA		3374 28CTGACAAG	_
[10614] ttctcttggttgtag *	3375 AATTTCAG	Exon	3437 29CTGGAAAA	[10679 * gtatgtt
[11561] catttctcatttcag *	3438 CCTAAAAC	Exon		[11709] * gtaagtg
[15476] tgtctgtattaaaag *			3689 31TTGTAAGG	
_21107] tttttttttcccctag *	3690 TCTGAATT	Exon		[21548] * gtaagca
[21640] tcttccccaaagcag *	4130 AGCAGAAT	Exon		[21866] * gtaagat
[26002]ctttccttttaag *		Exon	5253 34GAATGAGT	[26902] * (poly-A)

FIG. 5-3